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Neurogenic lower urinary tract dysfunction (NLUTD) in patients with spinal cord injury:

long-term urodynamic findings

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Bladder function of spinal cord injury patients in the long-term: a longitudinal urodynamic study

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Abstract

Objectives: To investigate bladder function of spinal cord injury (SCI) patients in the long-term since morbidity and mortality of SCI patients are closely related to bladder function but long-term data are scarce.

Subjects/patients and methods: A consecutive series of 246 SCI patients with neurogenic lower urinary tract dysfunction (NLUTD) was evaluated at a single university spinal cord injury center in a longitudinal study. Patients were prospectively evaluated since 2010 and compared retrospectively to the eldest urodynamic examination which could be found in the archive with a mean follow-up period of 6 years.

Results: Mean age at injury and mean duration of lesion were 51 ± 14 and 17 ± 10 years, respectively.55% (163/246) of the patients had a thoracic SCI and 21% (51/246), 18% (44/246) and 2% (6/246) had a cervical, lumbar and sacral lesion, respectively. In the most current (and eldest examination), most patients 147/246 (131/246) relied on intermittent self-catheterization, 65/246 (89/246) voided spontaneously and 49/246 (43/246) had an indwelling catheter. 147/246 (168/246) patients had no urological medication, the remaining 99/246 (78/246) were under antimuscarinics or alpha-blockers and/or underwent regular botulinum neurotoxin type A (BoNTA) intra detrusor injections. Mean maximum cystometric capacity, maximum detrusor pressure during the storage phase and bladder compliance were 650 mL (440mL), 34 cmH2O (25cmH2O) and 95 mL/cmH2O (55mL/cmH2O), respectively. Detrusor overactivity was found in 130/246 (59/246) and vesico-uretero-renal reflux (grade I or II) in 12/246 (11/246) patients (unilateral in 5 (9), bilateral in 7 (2)).

Conclusions: Most of our regularly followed patients with NLUTD due to SCI for a mean of 17 years had normal maximum cystometric capacity, maximum detrusor pressure during the storage phase, and bladder compliance. Vesico-uretero-renal reflux was quite rare and low grade. Thus, regular follow-up with urodynamic investigation allowing for individual bladder management seems beneficial warranting randomized longitudinal studies.

Introduction

Spinal cord injury (SCI) often causes neurogenic lower urinary tract dysfunction (NLUTD)(1). Neuro-urological care aims preservation or improvement of upper urinary tract function, control of urinary tract infection, and maintenance of a low-pressure bladder that is both continent and capable of emptying completely(2). These goals are ideally achieved without an indwelling catheter or a stoma, and in a manner that is socially and vocationally acceptable to the patient avoiding complications such as recurrent urinary tract infections, urethral strictures, calculus disease, hydronephrosis, and renal failure(2). In the past, renal disease was responsible for almost 50% of deaths in SCI patients(3). Fortunately, this changed dramatically. Nowadays, urinary disease accounts for only about 13% of deaths in SCI patients whereas pneumonia, influenza, non-urinary tract septicemia, cancer, and ischemic heart disease are more common causes of death(4, 5). The introduction of intermittent self-catheterization (ISC) combined with antimuscarinic treatment and the use of regular urodynamic investigations revolutionized the care of SCI patients(6-8). Thus, adequate function of the lower urinary tract is essential to prevent morbidity and mortality in SCI patients, but publications investigating bladder function of these patients in the long-term are scarce. We therefore assessed the long-term data of a strictly urodynamic-based treatment regime in patients with NLUTD due to SCI.

Patients & Methods

Ethics statement

This study was approved by the local ethics committee (i.e. the Kantonale Ethikkommission Zürich, Switzerland, study identification number: EK 2010-0207/01) and registered with ClinicalTrials.gov (study registration number: NCT01297660). All participants gave written informed consent.

Patients

From January 2010 to June 2014, 246 SCI patients were prospectively evaluated at the Spinal Cord Injury Center, Balgrist University Hospital, Zürich. The obtained data of the current examination was compared retrospectively to the eldest urologic examination including an urodynamic examination which could be found in the archive. Inclusion criteria were NLUTD due to SCI and duration of SCI of at least 5 years. Pregnant and breast feeding women and patients <18 years old at last evaluation were excluded.

All methods, definitions, and units are according to the standards recommended by the International Continence Society(9).

Neuro-urological evaluation

Neuro-urological evaluation consisted of medical history, clinical examination, urinalysis, urine culture, urinary tract ultrasound, and video-urodynamic investigation including pelvic floor electromyography(1). Video-urodynamics were performed using a multichannel system according to good urodynamic practices standard procedure recommended by the International Continence Society(10, 11). Patients were urodynamically investigated in a sitting position whenever possible. The bladder was filled with a 36°C mixture of 0.9% sodium chloride solution and contrast medium at a speed of 20mL/min.

Outcome measures

Primary outcome measures were urodynamic parameters including maximum cystometric capacity, maximum detrusor pressure during the storage phase, bladder compliance, detrusor overactivity, and detrusor leak point pressure. Secondary outcome measures were vesico-uretero-renal reflux (VUR) and urinary tract ultrasound. Normal renal parenchyma thickness was defined as >12mm, determined by the coronal measure of the distance between the renal sinus/parenchyma interface and the renal surface(12).

Tertiary outcome measure was the urinary continence status including the pads used per 24 hours as assessed by a 3-day bladder diary.

Statistical analyses

Data were approximately normal distributed and presented as mean ± standard deviation (SD). Comparing related and unrelated samples, the paired and unpaired t test was used. The value of significance was considered at $p<0.05$. Statistical analyses were performed using GraphPad Prism, version 6.01 (GraphPad Software, CA, USA).

Results

Of the 246 patients enrolled almost four out of five were men. The biggest group of patients suffered from thoracic spinal cord injury and ASIA impairment score grade A, i.e. complete lesion with no sensory or motor function preserved (http://www.asia-spinalinjury.org).Mean duration since SCI to most current examination was 17 ± 10 and mean age of patients at that time was 51 ± 14 years. (for detailed patient characteristics please see Table 1)

The mean follow up time between the most current and most eldest examination was 6 ± 3 years.

The most common type of bladder emptying is the clean intermittent self-catheterization (ISK). The total number of patients treated with indwelling catheters remains among the age of SCI about the same with one out of five. Whereas spontaneous voiding declined by 10% (24 patients). (for detailed bladder emptying characteristics please see Table 2) At the most current examination 80 patients (33%) suffered from urinary incontinence. Of these, 27 (11%) persons used one pad per day and 22 patients required 2 or more pads per 24 hours.

The numbers of patients with urological treatments remained about the same among the years (details in Table 3). Two out of three patients have no urological medication, one out of four is treated by antimuscarinics and one third of patients receives Botulinum A toxin (BoNTA) injections into the detrusor. This rate increased impressive by 51 patients (264%).

Mean maximum cystometric capacity, mean maximum detrusor pressure during the storage phase, and mean bladder compliance were within the normal range(see details in Table 4). Video-urodynamic findings changed over the years significant, but remained all within the normal range (see details in Table 4). Mean maximum cystometric capacity and mean maximum detrusor pressure during storage phase increased by 210 mL and 9 cmH_2O, respectively. Mean compliance rose by 40 mL/cmH_2O while mean detrusor leak point pressure decreased by 25 cmH_2O. Addidtional 71 patients (29%) suffered on the most currend examination from detrusor overactivity, what means an increase by 220%. Furthermore, detrusor overactivity related to incontinence increased by 13% (33 patients).

The total number of patients suffering from vesicoureterorenal reflux remained about the same (details in Table 5). However the number of unilateral reflux drops by 4 patients, while the number of patients with bilateral reflux rose by 7 patients. In addition there was one case with a unilateral reflux grade IV and one with a bilateral reflux grade III on both sides on the most current examination.

Discussion

Main findings

Most of our regularly followed patients suffering from NLUTD due to SCI for a mean of 17 ± 10 years had normal maximum cystometric capacity, maximum detrusor pressure during the storage phase, and bladder compliance. VUR was quite rare and low grade. On the most current examination, less patients used spontaneous voiding and relied instead on clean intermittent self-catheterization or indwelling catheter instead.

The use of urological medication in general increased, in particular the injections of BoNTA into the detrusor is increased 2.6 folds. Nevertheless Antimuscarinics were slightly less frequently used. Mean maximum detrusor pressure during storage rose and more patients suffered from detrusor overactivity. Considering the findings of the present study, regular follow-up including urodynamic investigations seems warranted since this allows for an individual bladder management preserving / improving lower and upper urinary tract function.

Findings in the context of existing evidence

Morbidity and mortality of SCI patients are closely related to bladder function. Elevated bladder pressure during the storage phase, either due to low-compliance bladder or detrusor overactivity, is the major cause of renal deterioration(13).In addition, older patients and those with a longer duration since SCI have a substantially higher risk for urological complications(14). At late stage post SCI, a high probability of change in the bladder management methods was reported indicating the importance of long-term planning from the time of SCI to minimize late complications(14). Indeed, since neuro-urological management evolved from reflex voiding and indwelling catheters to the widespread use of regular urodynamics, ISC, and antimuscarinics, optimized bladder management significantly contributed to the improved outcomes in SCI patients(15-17) with an enormous decrease of morbidity and mortality due to urological complications(2, 4, 5, 14).This is in line with the present longitudinal study showing urodynamic findings mostly within the normal range.

Most of our patients underwent regular BoNTA intra detrusor injections and/or were on antimuscarinics(18). Antimuscarinics are the pharmacological first-line treatment for overactive bladder and all currently used antimuscarinics have well-established efficacy shown in systematic reviews(8, 19, 20), Although BoNTA injections into the detrusor have become a popular, well-accepted second-line treatment with a recent FDA approval in August 2011 for refractory neurogenic detrusor overactivity incontinence(21, 22), several important issues such as optimal dosage and injection technique, timing for repeat injection, short- and long-term safety, and exact mechanisms of action remain to be elucidated(23).

Implications for practice

Our treatment strategy is based on urodynamic findings and this is supported by a retrospective study of 80 SCI patients reporting that only urodynamic measurements are reliable to prevent upper urinary tract deterioration, since bladder function is unpredictable by other parameters(7).Based on the pattern of dysfunction, a therapeutic strategy should aim to preserve both upper and lower urinary tract function and to attain urinary continence. This can be achieved in patients with detrusor overactivity and detrusor sphincter dyssynergia by converting the overactive into an underactive detrusor by antimuscarinics and to assist or accomplish bladder emptying by ISC. If this cannot be achieved by antimuscarinics, BoNTA intra detrusor injections or rarely bladder augmentation or urinary diversion are considered. In patients with underactive/ acontractile detrusor and detrusor sphincter dyssynergia ISC is recommended. If some patients are not able and/or not willing to perform ISC an indwelling transurethral or suprapubic catheter should be used instead of passive voiding by abdominal straining (Valsalva maneuver) or by suprapubic downwards compression of the lower abdomen (Credé maneuver).This creates unphysiologically high intravesical pressures which put the upper urinary tract at risk and also cause compression of the urethra, i.e. a functional obstruction leading to inefficient emptying. Thus, in accordance with the literature(16, 24-26), most of our patients relied on ISC. Recently, several authors(15, 27) found the suprapubic catheter a valuable treatment option in SCI patients. Although there is a lack of high-evidence level studies, we also support this view and prefer a suprapubic instead of a transurethral catheter. In the case of stress urinary incontinence due to decreased bladder outlet resistance, electrostimulation of the pelvic floor musculature may help to restore urinary continence in patients with incomplete lesions. In most patients with neurogenic stress urinary incontinence, however, the implantation of a suburethral sling or an artificial urinary sphincter may be necessary although this was not the case in the present study. Generally, artificial urinary sphincters are associated with a high revision rate but in SCI patients the modified “Nottwil technique” has been shown to be highly successful, reliable, safe, and even cost-effective(28).

Implications for research

Despite the management of NLUTD improved dramatically resulting in a substantial decrease of morbidity and mortality in SCI patients, many important issues remain to be elucidated. Thus, the patho-mechanisms involved in NLUTD are still incompletely understood. Indeed, SCI is not a stable chronic disease and modification of bladder management was necessary in more than one fourth of 196 SCI patients followed prospectively for 6 years(14). Electrophysiological and structural / biochemical changes during the long-term course of SCI patients may provide new insights into NLUTD warranting appropriately designed longitudinal studies applying a holistic approach, i.e. clinical, urodynamical, electrophysiological, structural/biochemical, and neuro-radiological assessments. Developing biomarkers for SCI patients guiding assessment, treatment and surveillance of NLUTD would be of great interest and could completely revolutionize modern neuro-urology. Nerve growth factor may become a clinically important biomarker and preliminary findings are promising(29). In addition, currently available treatment options need to be improved and new therapeutic targets have to be identified. Sacral neuromodulation(30) is a promising therapy but efficacy and safety have to be proven in randomized trials before more widespread use in SCI patients can be recommended(31).

Limitations of the study

Several limitations of the present study should be addressed. First, our study was not randomized and additional partly retrospective. Although it was longitudinal and the data of the current examination was gathered prospectively since 2010, the Data of the eldest examination had to be obtained retrospectively. Second, quality of life was not systematically assessed and could therefore not be evaluated. However, based on this study's findings, we introduced the Qualiveen questionnaire(32) in our routine neuro-urological work-up. Third, our patients underwent regular urinary tract ultrasound and video-urodynamics but not routine creatinine clearance and/or nuclear renal scan. It should be considered, however, that creatinine clearance has little value as a screening measure for renal disease in SCI patients because of its variability in serial testing(33). In addition, in the case of sonographically normal renal parenchyma and no VUR in the video-urodynamic investigation, the value of a nuclear renal scan is unclear. In fact, there is no generally agreed diagnostic tool/procedure to assess renal function of SCI patients in regular follow-up.

Conclusions

Most of our regularly followed patients suffering from NLUTD due to SCI for a mean of 17years had normal maximum cystometric capacity, maximum detrusor pressure during the storage phase, and bladder compliance. VUR was quite rare and low grade. Thus, regular follow-up with urodynamic investigation allowing for individual bladder management seems beneficial warranting randomized longitudinal studies.

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Conflict of interest

None of the authors has a conflict of interest with this study.

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References

1. Pannek J, Blok B, Castro-Diaz D, Del Popolo G, Groen J, Karsenty G, et al. EAU Guidelines on Neuro-Urology. 2014;http://www.uroweb.org/gls/pdf/21%20Neuro-Urology_LR.pdf.

2. Gormley EA. Urologic complications of the neurogenic bladder. Urol Clin North Am. 2010;37(4):601-7. Epub 2010/10/20.

3. Hackler RH. A 25-year prospective mortality study in the spinal cord injured patient: comparison with the long-term living paraplegic. J Urol. 1977;117(4):486-8.

4. Lidal IB, Snekkevik H, Aamodt G, Hjeltnes N, Biering-Sorensen F, Stanghelle JK. Mortality after spinal cord injury in Norway. J Rehabil Med. 2007;39(2):145-51.

5. Soden RJ, Walsh J, Middleton JW, Craven ML, Rutkowski SB, Yeo JD. Causes of death after spinal cord injury. Spinal Cord. 2000;38(10):604-10.

6. Lapides J, Diokno AC, Silber SJ, Lowe BS. Clean, intermittent self-catheterization in the treatment of urinary tract disease. J Urol. 1972;107(3):458-61.

7. Nosseir M, Hinkel A, Pannek J. Clinical usefulness of urodynamic assessment for maintenance of bladder function in patients with spinal cord injury. Neurourology and urodynamics. 2007;26(2):228-33.

8. Chapple CR, Khullar V, Gabriel Z, Muston D, Bitoun CE, Weinstein D. The effects of antimuscarinic treatments in overactive bladder: an update of a systematic review and meta-analysis. Eur Urol. 2008;54(3):543-62.

9. Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, et al. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. Neurourology and urodynamics. 2002;21(2):167-78.

10. Schafer W, Abrams P, Liao L, Mattiasson A, Pesce F, Spangberg A, et al. Good urodynamic practices: uroflowmetry, filling cystometry, and pressure-flow studies. Neurourology and urodynamics. 2002;21(3):261-74.

11. Gammie A, Clarkson B, Constantinou C, Damaser M, Drinnan M, Geleijnse G, et al. International Continence Society guidelines on urodynamic equipment performance. Neurourology and urodynamics. 2014;33(4):370-9. Epub 2014/01/07.

12. Edell SL KA, Rifkin MD. Normal renal ultrasound measurements. In: Goldenberg BB KA, editor. Atlas of ultrasound measurements. Chicago: Year Book Medical Publishers; 1990. p. 146.

13. McGuire EJ, Woodside JR, Borden TA, Weiss RM. Prognostic value of urodynamic testing in myelodysplastic patients. J Urol. 1981;126(2):205-9.

14. Drake MJ, Cortina-Borja M, Savic G, Charlifue SW, Gardner BP. Prospective evaluation of urological effects of aging in chronic spinal cord injury by method of bladder management. Neurourology and urodynamics. 2005;24(2):111-6.

15. Feifer A, Corcos J. Contemporary role of suprapubic cystostomy in treatment of neuropathic bladder dysfunction in spinal cord injured patients. Neurourology and urodynamics. 2008;27(6):475-9.

16. Hansen RB, Biering-Sorensen F, Kristensen JK. Bladder emptying over a period of 10-45 years after a traumatic spinal cord injury. Spinal Cord. 2004;42(11):631-7.

17. Pannek J, Kullik B. Does optimizing bladder management equal optimizing quality of life? Correlation between health-related quality of life and urodynamic parameters in patients with spinal cord lesions. Urology. 2009;74(2):263-6.

18. Wöllner J, Kessler TM. Botulinum toxin injections into the detrusor. BJU Int. 2011;108(9):1528-37. Epub 2011/10/26.

19. Novara G, Galfano A, Secco S, D'Elia C, Cavalleri S, Ficarra V, et al. A systematic review and meta-analysis of randomized controlled trials with antimuscarinic drugs for overactive bladder. Eur Urol. 2008;54(4):740-63. Epub 2008/07/18.

20. Buser N, Ivic S, Kessler TM, Kessels AG, Bachmann LM. Efficacy and adverse events of antimuscarinics for treating overactive bladder: network meta-analyses. Eur Urol. 2012;62(6):1040-60. Epub 2012/09/25.

21. Cruz F, Herschorn S, Aliotta P, Brin M, Thompson C, Lam W, et al. Efficacy and safety of onabotulinumtoxinA in patients with urinary incontinence due to neurogenic detrusor overactivity: a randomised, double-blind, placebo-controlled trial. Eur Urol. 2011;60(4):742-50. Epub 2011/07/30.

22. Ginsberg D, Gousse A, Keppenne V, Sievert KD, Thompson C, Lam W, et al. Phase 3 efficacy and tolerability study of onabotulinumtoxinA for urinary incontinence from neurogenic detrusor overactivity. J Urol. 2012;187(6):2131-9. Epub 2012/04/17.

23. Apostolidis A, Dasgupta P, Denys P, Elneil S, Fowler CJ, Giannantoni A, et al. Recommendations on the use of botulinum toxin in the treatment of lower urinary tract disorders and pelvic floor dysfunctions: a European consensus report. Eur Urol. 2009;55(1):100-19. Epub 2008/10/01.

24. Abrams P, Agarwal M, Drake M, El-Masri W, Fulford S, Reid S, et al. A proposed guideline for the urological management of patients with spinal cord injury. BJU Int. 2008;101(8):989-94.

25. Stohrer M, Blok B, Castro-Diaz D, Chartier-Kastler E, Del Popolo G, Kramer G, et al. EAU guidelines on neurogenic lower urinary tract dysfunction. European urology. 2009;56(1):81-8.

26. Dahlberg A, Perttila I, Wuokko E, Ala-Opas M. Bladder management in persons with spinal cord lesion. Spinal Cord. 2004;42(12):694-8.

27. Mitsui T, Minami K, Furuno T, Morita H, Koyanagi T. Is suprapubic cystostomy an optimal urinary management in high quadriplegics?. A comparative study of suprapubic cystostomy and clean intermittent catheterization. Eur Urol. 2000;38(4):434-8.

28. Bersch U, Gocking K, Pannek J. The artificial urinary sphincter in patients with spinal cord lesion: description of a modified technique and clinical results. Eur Urol. 2009;55(3):687-93. Epub 2008/04/09.

29. Liu HT, Chancellor MB, Kuo HC. Urinary nerve growth factor levels are elevated in patients with detrusor overactivity and decreased in responders to detrusor botulinum toxin-A injection. Eur Urol. 2009;56(4):700-6. Epub 2008/05/13.

30. Wöllner J, Hampel C, Kessler TM. Surgery Illustrated - surgical atlas sacral neuromodulation. BJU Int. 2012;110(1):146-59. Epub 2012/06/14.

31. Kessler TM, La Framboise D, Trelle S, Fowler CJ, Kiss G, Pannek J, et al. Sacral neuromodulation for neurogenic lower urinary tract dysfunction: systematic review and meta-analysis. Eur Urol. 2010;58(6):865-74.

32. Costa P, Perrouin-Verbe B, Colvez A, Didier J, Marquis P, Marrel A, et al. Quality of life in spinal cord injury patients with urinary difficulties. Development and validation of qualiveen. Eur Urol. 2001;39(1):107-13.

33. Sepahpanah F, Burns SP, McKnight B, Yang CC. Role of creatinine clearance as a screening test in persons with spinal cord injury. Arch Phys Med Rehabil. 2006;87(4):524-8.

Table 1. Patient characteristics

Total number of patients	246
Gender (%)	
Female	55 (22%)
Male	191(78%)
Level of spinal cord Injury (%)	
Cervical	54 (22%)
Thoracic	138 (56%)
Lumbar	47 (19%)
Sacral	7 (3%)
ASIA - Impairment scale (%)	
A	116 (47%)
B	34(14%)
C	29(12%)
D	64(26%)
Unknown	3(1%)

Table 2. Type of bladder emptying according to lesion level

	At earliest available urodynamic investigation (n=246)	At latest available urodynamic investigation (n=246)
Intermittent self-catheterization	**128 (52%)**	**145 (59%)**
Cervical	18 (14%)	19 (13%)
Thoracic	75 (59%)	93 (64%)
Lumbar	29 (23%)	29 (20%)
Sacral	6 (5%)	4 (3%)
Spontaneous voiding	**75 (30%)**	**52 (21%)**
Cervical [I]	20(27%)	18 (35%)
Thoracic [II]	40 (53%)	19 (37%)
Lumbar [III]	14 (19%)	12 (23%)
Sacral	1 (1%)	3 (6%)
Indwelling catheter	**43 (18%)**	**49 (20%)**
Cervical	16 (37%)	16 (33%)
Thoracic	23 (54%)	27 (55%)
Lumbar	4 (9%)	6 (12%)
Sacral	-	-

[I]including 8 and 5 patients relying on a condom catheter at earliest and latest available urodynamic investigation, respectively
[II]including 14 and 2 patients relying on a condom catheter at earliest and latest available urodynamic investigation, respectively
[III]including 2 and 1 patients relying on a condom catheter at earliest and latest available urodynamic investigation, respectively

Table 3. Neuro-urological medication according to lesion level

	At earliest available urodynamic investigation (n=246)	At latest available urodynamic investigation (n=246)
None	**158(64%)**	**131 (54%)**
Cervical	33 (21%)	28 (21%)
Thoracic	86 (55%)	69 (53%)
Lumbar	32 (20%)	28 (21%)
Sacral	7 (4%)	6 (5%)
Alpha-blockers	**5 (2%)**	**5 (2%)**
Cervical	1 (20%)	1 (20%)
Thoracic	3 (60%)	2 (40%)
Lumbar	1 (20%)	2 (40%)
Sacral	-	-
Antimuscarinics	**53 (22%)**	**28 (11%)**
Cervical[I]	9 (17%)	4 (14%)
Thoracic[II]	34 (64%)	18 (64%)
Lumbar[III]	10 (19%)	5 (18%)
Sacral	-	1 (4%)
OnabotulinumtoxinA injections into detrusor	**30 (12%)**	**82 (33%)**
Cervical [IV]	11 (37%)	21 (25%)
Thoracic [V]	15 (50%)	49 (60%)
Lumbar[VI]	4 (13%)	12 (15%)
Sacral	-	-

[I]including 2 and 0 patients takingaddition an a alpha-blockerat earliest and latest available urodynamic investigation, respectively
[II]including 1 and 2 patients takingaddition an a alpha-blocker at earliest and latest available urodynamic investigation, respectively
[III]including 1 and 2 patients takingaddition an a alpha-blocker at earliest and latest available urodynamic investigation, respectively
[IV]including 6 and 7 patients takingaddition an aantimuscarinic drug at earliest and latest available urodynamic investigation, respectively
[V]including 4 and 9 patients takingaddition an aantimuscarinic drug at earliest and latest available urodynamic investigation, respectively
[VI]including 2 and 0 patients takingaddition an aantimuscarinic drug at earliest and latest available urodynamic investigation, respectively

Table 4. Video-urodynamic findings

	At earliest available urodynamic investigation (n=246)	At latest available urodynamic investigation (n=246)	p
Maximum cystometric capacity in mL (mean ± SD)	440 ± 180	650 ± 355	<0.0001
Compliance in mL/cmH_2O (mean ± SD)	55 ± 40	95 ± 88	<0.0001
Maximum detrusor pressure during storage phase in cmH_2O (mean ± SD)	25 ± 17	34 ± 27	0.008
Detrusor overactivity	59 (24%)	130 (53%)	<0.0001
- with incontinence	32 (13%)	56 (23%)	
- detrusor leak point pressure in cmH_2O (mean ± SD)	49± 23	32 ± 25	
Detrusor sphincter dyssynergia	72 (30%)	61 (25%)	0.001
Vesico-uretero-renal reflux	11 (4%)[I]	12 (5%)[II]	0.99
- Grad 1-3	11 (4%)	11 (4%)	
- Grad 4-5	0 (0%)	1 (0%)	

[I]Including2 patients (1%) with bilateral reflux

[II]Including 7 patients (3%) with bilateral reflux